BIOCHEMICAL CHANGES ASSOCIATED WITH CHRONIC HEPATITIS-B-VIRUS INFECTION IN BABYLON PROVINCE

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Abstract:

This study was done to illustrate some biochemical changes in chronic hepatitis B viral (HBV) infection in Babylon district. Seventy patients with chronic hepatitis B viral infection were enrolled in this study which lasted from November (2007) to May (2008), and consists of (57 males) and (13 females) with a mean age of (31.5±7.8 years). Those patients were matched with thirty apparently healthy subjects (as controls), consisted of (21 males) and (9 females) with a mean age of (30.5±6.7 years). The investigations for those patients and controlled subjects were done in laboratory of Marjan Teaching Hospital, AL-Hilla Teaching Hospital and advanced physiology laboratory in Medical College of Babylon University. The results of this study ware as in the following: The mean value of aspartate aminotransferase (AST) for patients (45.33±8.25 IU/L) was higher than of controls (19.57±5.40 IU/L), also alanine aminotransferase (ALT) for patients (49.33±8.07 IU/L) was higher than of controls (16.47±4.51 IU/L). There were no significant differences between patients and controls for serum alkaline phosphatase (AP), and total serum bilirubin (TSB). The fasting blood sugar (FBS) for patients (8.25±1.95 mmol/L) was more than of controls (4.24±0.61 mmol/L)

المتغيرات الكيموحيوية المتزامنة مع التهاب الكبد الفيروسي نوع "ب" المزمن
في محافظة بابل

الخلاصة:
أعدت هذه الدراسة لتوضيح بعض المتغيرات الكيموحيوية عند المرضى المصابين بالتهاب الكبد الفيروسي نوع "ب" المزمن في محافظة بابل. لقد شملت هذه الدراسة سبعين مريضا مصاب بالتهاب الكبد الفيروسي نوع "ب" المزمن والتي استمرت من تشرين الثاني 2007 ولغاية أيار 2008 المكونين من(57 من الذكور) و(13 من الإناث) وكان متوسط أعمارهم (31,5 سنة) وتم مقارنتهم بالأصحاء في مجموعة السيطرة والذي كان عددهم ثلاثون شخصا مكونين من (21 من الذكور) و(9 من الإناث) وكان متوسط أعمارهم (30,5 سنة).
لقد اجري للمرضى والأصحاء في مجموعة السيطرة تحليلات مختبريه في مستشفى مرجان التعليمي ومستشفى الحلة التعليمي ومختبر الدراسات العليا لفرع الفسلجة في كلية الطب- جامعة بابل وكانت النتائج كالأتي:
إن متوسط قيمة إنزيم ناقل أمين الاسبارتات (AST) للمرضى (45,33 وحدة\لتر) وهو أعلى من مجموعة السيطرة (19,57 وحدة\لتر) وكذلك متوسط قيمة إنزيم ناقل أمين الالانين (ALT) للمرضى (49,33 وحدة\لتر)وهو أعلى قيمة من مجموعة السيطرة (16,47 وحدة\لتر). لا يوجد اختلاف مهم بين المرضى والأصحاء بالنسبة إلى الفسفتاز القلوية (AP) وبليروبين المصل الكلي (TSB). إن متوسط قيمة سكر الدم للمرضى (8,25 ملي مول\لتر) أكثر من متوسط قيمته عند مجموعة السيطرة (4,24 ملي مول\لتر).

Introduction and Review of Literatures

Background:

Hepatitis B is a viral disease with a high incidence and prevalence worldwide and it can cause acute and chronic liver disease (Tsuyoshi and Nagayama, 2004). Approximately (8%) of the world's population has been infected with HBV, and about (350 million, 5–6%) are persistent carriers of HBV (Inlin, et al., 2005). The clinical presentation ranges from subclinical to symptomatic and, in rare instances, fulminant hepatitis (Parveen and Michael, 2006). Perinatal or childhood infection is associated with few or no symptoms, but it has a high risk of becoming chronic. There are limited number of medications that can be used to effectively treat chronic hepatitis B; a safe and effective vaccine is available to prevent hepatitis B infection (Alexander and Kourtis, 2007).

Investigation of chronic HBV:

1. Serum aminotransferase:

AST, also sometimes termed SGOT and ALT, also sometimes termed SGPT are widely distributed in cells throughout the body (Zheng, et al., 2008). AST is found primarily in heart, liver, skeletal muscle, and kidney, while ALT is found in liver and kidney, with lesser amounts in heart and skeletal muscle (Carol, 2007). Generally, serum ALT and AST levels reflect the extent of hepatocellular damage and are most frequently used to assess liver function. AST and ALT activity in liver are about 7,000 and 3,000 times serum activities, respectively and ALT is exclusively cytoplasmic; both mitochondrial and cytoplasmic forms of AST are found in all cells (Zhuang, 2007). In adults, AST and ALT activities are significantly higher in males than in females, and reference intervals vary with age until about age 15, AST activity is slightly higher than that of ALT, with the pattern reversing by age 15 in males but persisting till age 20 in females. In adults, AST activity tends to be lower than that of ALT until approximately age 60, when they become roughly equal and upper reference limits vary little between the ages of 25 and 60 years, so the age-adjusted reference limits need to be used for this population (Zheng, et al., 2008). Separate reference limits are needed for children and older adults; these may require national efforts to obtain enough samples from healthy individuals to accurately determine reference limits, liver disease is the most important cause of increased ALT activity and a common cause of increased AST activity (Nalpas, et al., 1994). (Olut, et al., 2007) found that in chronic HBV infection and during the one year period of the study that 89% of the patients yielded continuously normal ALT levels, while 11% showed at least one ALT value above the normal levels (ALT more than 1.2 time of normal value). Other study showed that, the serum ALT levels were constantly normal in 57.4% of patients HBV-DNA positive and above the normal in 42.6% of the patients (Myers, et al., 2003). In conclusion, although ALT levels may be normal, it should always be taken into consideration that more than half of inactive HBsAg carriers exhibited low level viral replication, thus HBV-DNA and liver enzyme levels should be monitored routinely in order not to miss the acute

manifestations (Olut, et al., 2007). A prospective study shows that the ALT and AST levels in chronic HBV infection were greater than 60 IU/L for the testing hospital before or at enrollment (Yu, et al., 2005). AST or ALT values less or equal 30IU/L excluded significant activity with 96% certainty. So the aminotransferases are accurate noninvasive markers of hepatitis B virus-related activity and fibrosis (Myers, et al., 2003). (Lai, et al., 2007) revealed in their study, were the patients divided into 3 groups; persistently normal ALT (PNALT); ALT 1-1.5 time the upper limit of normal (ULN), and ALT more than 1.5 time ULN and the results of this study; about 18% of patients with PNALT had stage 2 fibrosis and 34% had grade 2 or 3 inflammation, and overall 37% of patients with PNALT had significant fibrosis or inflammation; subgroup analysis showed the majority with fibrosis belonged to the high normal ALT group and that only a minority who were young and immune tolerant had significant findings on biopsy; there is significant fibrosis and inflammation in 37% of patients with PNALT and a liver biopsy should be considered in patients older than 40 with high normal ALT. Other study showed that the serum ALT and AST levels are usually elevated in patients with chronic hepatitis, although a small number of patients with histological chronic hepatitis have transiently normal aminotransferase levels (David and Daniel, 2003). Even mild elevation of aminotransferase levels (5-10 IU/L) higher than the upper limit of normal should lead the physician to consider the presence of chronic hepatitis, and elevation of more than 400 IU/L are common in the case of untreated sever chronic viral hepatitis (Lawrence, et al., 2005). In a study was done in Turkey the researchers founds that serum mean ALT values were elevated three to six times and mean AST values were approximately three times elevated in chronic hepatitis B (Kursad, et al., 2005). Another study was done on HCV revealed that the 15-50% of individuals with chronic hepatitis C infection had normal ALT and it was consistently higher than AST with all causes of chronic hepatic injury except alcohol; AST is normal in a significant number of cases, ALT may be normal in patients with cirrhosis, while AST remains elevated in a minority of individuals with only one elevated ALT had liver disease (Inglesby, et al., 1999). Patients with slightly elevated ALT (1-2 times the upper reference limit) are more likely to have transient elevation not due to disease; however, about 30% of those

with chronic HCV infection have peak ALT less than 2 times the upper reference limit. In patients with chronic HBV infection without elevated ALT “chronic carriers”, about10% will develop increased ALT on follow-up (Dufour, 1998). Other studies were done on patients with acute hepatitis who found that serum AST and ALT values were greater than 500 IU/L, with ALT being greater than AST (Flink, et al., 2006). The prevalence of elevated ALT was 28.5% in HBV, and elevation was more common in men compared to women (Chen, et al., 2007). (Veldhuijzen, et al., 2008) revealed that a single ALT determination can successfully predict viral load in chronic HBV patients and can be used in primary care to select patients for referral to specialist care. Some times patients with high serum HBV DNA but have a normal serum ALT activity, this occurs in cases known as (immunotolerant hepatitis B) (Wang, et al., 2008).

2. Serum alkaline phosphatase (AP):

AP is an enzyme involved in metabolite transport across cell membranes and is found in a decreasing order of abundance, in placenta, ileal mucosa, kidney, bone, and liver. Alkaline phosphatase share a common protein structure, coded by the same gene (Weiss, et al., 1998). Elevation of AP in the setting of liver disease results from increased synthesis and release of the enzyme into serum rather than from impaired biliary secretion and there are two primary categories of abnormal liver chemistry studies are hepatitis and cholestatic liver disease, and the cholestatic liver diseases primarily cause elevation of serum alkaline phosphatase values (Mark, et al., 1998). (Whitehead, et al., 1999) showed in a study done on patients with HBV, that the AP was over 3 times the upper reference limit in less than 10% of cases and about 90% of those patients had normal value. Another study was done for hepatitis revealed that the elevation of AP above normal limit was in less than 8% of cases (Doumas, et al., 2004).

3. Total serum bilirubin (TSB):

Daily production of unconjugated bilirubin is 250 to 350 mg, mainly from senescent erythrocytes clearance at normal values is 5 mg/kg/day, or about 400 mg/day in adults; the rate does not increase significantly with hemolysis (Chowdhury, et al.,

1995). The half-life of unconjugated bilirubin is less than 5 minutes, and delta bilirubin (also sometimes termed biliprotein) is produced by reaction of conjugated bilirubin with albumin and it has a half-life of about 17-20 days, accounting for prolonged jaundice in patients recovering from hepatitis or obstruction and total bilirubin rarely exceeds (4-5 mg/dl), even during prolonged fasting; unless other factors increasing bilirubin are also present and increases in conjugated bilirubin are highly specific for disease of the liver parenchyma or bile ducts (David and Daniel, 2003). Increased conjugated bilirubin may also occur with impaired energy-dependent bilirubin excretion in sepsis, total parenteral nutrition, and following surgery; the serum bilirubin level is associated with the extent of hepatocellular necrosis, elevated serum bilirubin levels should be differentiated from cholestatic liver disease that can occur both within and outside the liver (Zhuang, 2007). Serum bilirubin rises markedly and keeps rising in patients with liver failure, and the total serum bilirubin is often greater than 10 times ULN, and the daily increment is greater than 1time ULN, and sometimes, the bilirubin diverges from the aminotransferase levels (Mark, et al., 1998). Serum bilirubin level is normal (0.0-1.0 mg/dl) in chronic viral hepatitis, the frequency of jaundice in patients with acute viral hepatitis differs both by age and etiologic agent, and jaundice is rare in children than in adults and only 1% of children with acute hepatitis had peak bilirubin value over 171 mol/L (10 mg/dL), and only 27% of adults had, while in another study found that the jaundice develops in 70% of cases of acute hepatitis A (Hoofnagle, 1997). (Gitlin, 1997) in a study was done for acute hepatitis B and C viral infection revealed that jaundice develops in 33-50% of acute HBV and 20-33% of cases of acute hepatitis C. There is a direct correlation between age and peak serum bilirubin in children; an increase of 10 years in age was associated with an average increase of 85 mol/L (5 mg/dl) in bilirubin. In adults, there is no relationship between age and peak bilirubin, in addition to that the distribution of direct bilirubin as a percentage of total bilirubin is similar in acute hepatic injury and obstructive jaundice (Flink, et al., 2006).

4. Fasting blood sugar (FBS):

The study was done for HBV showed that diabetes mellitus was also significantly more frequent in chronic HBV infected patients (Kassas, 1997). (Paraschiv, et al., 2002) found that the frequency of diabetes and impaired glucose tolerance in chronic liver diseases was 30% in patients with HCV infection and 17% with HBV infection who showed an altered response to a standard oral glucose tolerance test. (Kwon, 2003) found that the impaired glucose tolerance and overt diabetes mellitus (DM) frequently occurs in patients with chronic liver disease, and among the cirrhotic patients 57.1% had HBV related disease and 10% had HCV related disease, and a DM was observed in 22.4% of the cirrhotic patients; and in the diabetic group, the frequency of HCV infection was significantly greater, and only 20.6% of the diabetic patients had normal range blood glucose levels even though most of them received medical therapy. Also diabetic patients, the cases with well controlled blood glucose, showed higher survival rate than poorly controlled cases. (Arao, et al., 2003) revealed that the prevalence of DM was higher in HCV- infected patients (20.9%) than in HBV-infected subjects (11.9%) and in the case-control study of the diabetic patients, 10.5% of patients were infected with type C hepatitis compared with 1.1% with type B hepatitis. (Kwon, et al., 2005) showed that the prevalence of DM was 19.7% in the HBV, and the DM was detected before the diagnosis of cirrhosis or simultaneously in 79% of HBV. (Papatheodoridis, et al., 2006) found that the diabetes was present in (13%) of chronic hepatitis patients, without any difference between those with chronic hepatitis B (14%) or chronic hepatitis C (13%), and the presence of diabetes was independently associated with more severe fibrosis or presence of cirrhosis. In a previous study the researchers illustrated that the prevalence of diabetes mellitus was significantly higher in patients with HBV than in those without HBV (58.9% vs. 33.3%), and the prevalence of diabetes mellitus in patients with HBV was significantly higher than in those without HBV among Asians (65.0% vs. 27.5%) but not in Pacific Islanders (43.8% vs. 37.1%, P=0.60), and in patients who were tested for both HBV and HCV, the prevalence of diabetes mellitus was 29.4% in uninfected subjects, 44.4% in patients with HBV monoinfection, 47.2% in patients with HCV monoinfection and 85.0% in patients with HBV and HCV coinfection, so HBV infection is strongly associated with diabetes

mellitus among Asians, Americans, but not in Pacific Islanders, whereas HCV infection was associated with diabetes mellitus in both ethnic groups. Asians have a higher prevalence of both diabetes mellitus and chronic hepatitis B infection compared to Caucasians (Ling, et al., 2007). (Imazeki, et al., 2008) found that the prevalence of DM in the chronic HBV, and chronic HCV groups was 6.3%, and 13.6%, respectively. Other studies revealed that the HBV was detected in 11% of the diabetic patients and in 3% of the controls. These data suggest that the prevalence of occult HBV infection is higher in diabetics compared with healthy controls and this may contribute to the increased prevalence of primary hepatocellular carcinoma in diabetics (Demir, et al., 2008).

The aim of this study:

Chronic HBV is associated with many anatomical, epidemiological, physiological, biochemical and immunological changes. Owing to the fact that insufficient informations concerning the effect of these factors on Iraqi patients are available, this study was carried out to provide insight to this question and to know some physiological changes in Iraqi patients. Such information is of no doubt necessary as a background for any programs devised in the future for studying chronic HBV, and treating this disease. Also this study will aid in gaining a better understanding of the pathogenesis of the chronic HBV, and this ultimately leads to advances in the design of drugs of choice to prevent and treat this disorder. To fulfill these objectives, the present study has dealt with samples of subjects in Babylon province to determine:

1. AST
2. ALT.
3. AP.
4. TSB.
5. FBS.

Materials and Methods

A. Materials:

1. Subjects of the study:

1.1. Patients:

Seventy patients were included in this study which lasted from November (2007) to May (2008), and consisted of (57 males) and (13 females). The mean age of those patients was (31.5±7.8 years). Those patients were attended to the gastroenterology center in the Marjan teaching hospital and diagnosed by specialist doctors as chronic hepatitis B infection.

The epidemiological distribution of those patients was as the following: The residency (49 urban and 21 rural area), marital status (51 married and 19 single), economic status (14 good, 16 medium and 40 low level), educational level (9 high education levels and 61 low educational levels), history of smoking (44 with positive history and 26 with negative history), alcohol intake (60 not alcoholic while 10 alcoholic) and all patients included in this study have no history of drugs addiction.

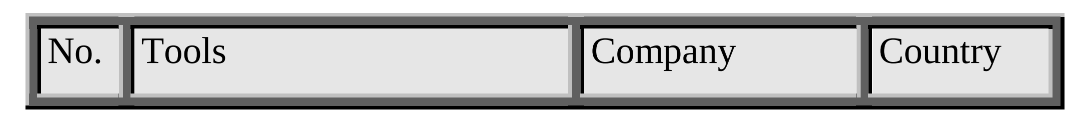
1.2. Controls:

Thirty apparently healthy subjects (clinically assessed by specialist doctors) were included as controls in this study, which consist of (21 males) and (9 females). The mean age of those subjects was (30.5±6.7 years). Those subjects were selected randomly from the population.

The epidemiological distribution of those subjects was as the following: The residency (23 urban and 7 rural area), marital status (19 married and 11 single), economic status (4 good, 9 medium and 17 low level), educational level (4 high education, 26 low education), history of smoking (21 with positive history and 9 with negative history), alcohol intake (26 not alcoholic while 4 alcoholic) and all subjects enrolled in this study have no history of drugs addiction.

2. Instruments:

Table (2-1): The tools used in this study and their sources



No.	Tools	Company	Country

2.	Micro-pipette	Oxford,	USA
4.	Plain tubes	Afma-dispo	Jordan
5.	Disposable syringes	Witeg	Malaysia

Table (2-2): The main instruments used throughout the study and their sources

No.	Instruments	Company	Country
3.	Water bath	Memmert	Germany
4.	Centrifuge	Hermle	Japan
5.	Spectrophotometer	Cecil	England
6.	Refrigerator	Concord	Lebanon
7.	Incubator	Memmert	Germany
8.	Water distillator	G.F.L.	Germany

3. Chemicals:

Table (2-3): The chemical and biological materials used throughout the study and their sources

No.	Chemical materials	Company	Country
1.	AST- kit	Randox	U. K.
2.	ALT- kit	Randox	U. K..
3.	AP -kit	Biomerieux	France.
4.	Bilirubin- kit	Human	Germany
5.	Glucose -kit	Human	Germany
6.	HBsAg-kit	Biokit	Spain

7.	HCV-kit	Biokit	Spain

B. Methods :

1. Blood collection:

The collection of blood was done in gastroenterology center in the Marjan teaching hospital at (9-12:am). The brachial vein on the front of the elbow was employed. The arm should be warm to improve blood circulation and distended the vein. A tourniquet was applied directly on the skin around the arm (usually from the left arm), approximately (6-8cm) above the site of collection. The skin over the vein was sterilized with a small pad of cotton wool soaked with 70% ethyl alcohol, and the site was dried with clean gauze to prevent hemolysis. Needles used were 21 gauge. Two groups of labeled tubes were used; the first tubes contain disodium ethylene diamine tetra acetic acid (EDTA) as anticoagulants to prevent clotting of blood to be used for hematological studies. The second group tubes were without anti-coagulant as plain tubes, for blood to be used for preparing sera for subsequent biochemical tests. The blood was allowed to clot for 15 minutes, the clot shrinks and screw can be obtained by centrifugation and precautions were taken to avoid hemolysis. The serum samples were liquated in sterile test tubes using micropipette with sterile disposable tips. Each sample was labeled and given a serial number together with the patient name, the serum samples were frozen at (-20°C) for biochemical analysis (Lewis, et al., 2006).

The investigations for those patients and control group were done in the laboratory of Marjan Teaching Hospital and post graduate physiology laboratory of medical college of Babylon university.

3.1. Determination of AST:

Colorimetric method was used to measure the amount of oxaloacetic acid produced under fix conditions. A reddish brown by hydrazone formed when 2,4 dinitrophenyl hydrazine in alkaline solution was added and measured at 530-550 nm by

the spectrophotometer according to procedure recommended by the company (Randox, UK) (Reitman and Frankel, 1957).

3.2. Determination of ALT:

Colorimetric method was used for the determination of GPT reaction with 2,4 dinitrophenyl hydrazine in alkaline solution, a brown colored hydrazone was formed and measured by using spectrophotometer at 490-560 nm as procedure recommended by the company (Random, UK) (Reitman and Frankel, 1957).

3.3. Determination of AP:

The method used was that in which phenyl phosphate is hydrolyzed with the liberation of phenol and formation of phosphate. The amount of phenol which formed was estimated colorimetrically by using spectrophotometer at 510 nm according to the procedure recommended by the company (Biomerieux, France) (Kind and King, 1954).

3.4. Determination of TSB:

Working solution was prepared by mixing reagent 1(RI) with reagent 3 (R3); mix well and incubate exactly for 5 minutes at 37°C and read at wave length 555 nm by using spectrophotometer according to the procedure recommended by the company (Human, Germany) (Walter and Gerarde, 1970).

3.5. Determination of FBS:

The glucose is determined after enzymatic oxidation in the presence of glucose oxidase. The formed hydrogen peroxide reacts under catalysis of peroxidase with phenol and 4-aminophenazone to a red-violet quinoneimine dye as indicator. The absorbance of standards and samples are measured against reagent blank at 546nm according to the procedure recommended by the company (Human ,Germany) (Dingeon, 1975).

C. Statistical analysis:

All values were expressed as means ± SD. The data were analyzed by using of SPSS program and taking $p < 0.05$ as the lowest limit of significance. Student's t-test was used to examine the differences between different groups. Both t-test, chi square and ANOVA test were applied to determine the differences between one group and another, and between all groups and within group (Wayne, 1999)..

The Results

3.1. AST:

The mean values of AST for patients enrolled in this study was (45.33±8.25 IU/L), whereas in control group it was (19.57±5.40 IU/L). There were a significant ($P < 0.05$) difference between patients and control group. (Table 3-3).

Table (3-3): Mean values of AST (IU/L) for patients and control group.

AST		Mean ± S.D.	No.
Groups	patients	45.33 ± 8.25	70
	Control	19.57 ± 5.40	30
Total			100

Significant differences between patients and control group ($P < 0.05$).

3.8. ALT:

The mean values of ALT for patients was (49.33±8.07 IU/L), compared to (16.47±4.51 IU/L) in control group. Significant differences ($P < 0.05$) between patients and control group were found. (Table 3-4).

Table (3-4): Mean values of ALT (IU/L) for patients and control group.

ALT		Mean ± S. D.	No.
Groups	patients	49.33 ± 8.07	70
	Control	16.47 ± 4.51	30
Total			100

Significant differences between patients and control group (P < 0.05).

3.13. AP:

There were insignificant differences (P > 0.05) between patients and control group, and the mean values of AP for patients was (51.34±12.03 IU/L), and for control group it was (50.43±9.99 IU/L). (Table 3-5).

Table (3-5): Mean values of AP (IU/L) for patients and control group.

AP		Mean ± S. D.	No.
Groups	patients	51.34 ± 12.03	70
	Control	50.43 ± 9.99	30
Total			100

No significant differences between patients and control group (P > 0.05).

3.14. TSB:

This study revealed that there was in significant (P > 0.05) statistical differences in the mean values of TSB for patients (11.71±3.89 µmol /L), and control group (10.43±3.99 µmol /L). (Table 3-6).

Table (3-6): Mean values of TSB (µmol/L) for patients and control group

TSB		Mean ± S. D.	No.
Groups	patients	11.71 ± 3.89	70
	Control	10.43 ± 3.99	30
Total			100

No significant differences between patients and control group (P >0.05).

3.15. FBS:

This study revealed that there was a significant difference (P < 0.05) between the mean values of FBS for patients (8.25±1.95 mmol/L), and control group, (4.24±0.61 mmol/L). (Table 3-7).

Table (3-7): Mean values of FBS (mmol/L) for patients and control group.

FBS		Mean ± S. D	No.
Groups	patients	8.25 ± 1.95	70
	Control	4.24 ± 0.61	30
Total			100

Significant differences between patients and control group (P < 0.05).

Discussion

4.9. AST and ALT:

The mean values of AST for patients enrolled in this study is (45.33±8.25 U/L), while in control group it is (19.57±5.40 U/L), and the mean values of ALT for patients is (49.33±8.07 U/L), while for control group it is (16.47±4.51 U/L). The results of present study indicated that, the aminotransferase enzymes will mildly elevate in chronic HBV infection and this finding is consisted with other study done by (Olut, et al., 2007), who found that in chronic HBV infection and during the one year period of study 89% of the patients yielded continuously normal ALT levels, while 11% showed at least one ALT value above the normal levels (ALT more than 1.2 time of normal value). (Myers, et al., 2003) revealed that, the serum ALT levels are constantly normal in 57.4% of patients were HBV-DNA positive and above the normal in 42.6% of the patients. This study is in agreement with other a prospective study done by (Yu, et al., 2005); who showed that the ALT and AST levels in chronic HBV infection was about

60 IU/L for the testing hospital before or at enrollment. (Lai, et al., 2007) revealed in a study done on the chronic HBV, the incidence of ALT values increase with increment hepatic fibrosis, and a liver biopsy should be considered in patients with high normal ALT. Another study showed that the serum ALT and AST levels are usually elevated in patients with chronic hepatitis, although a small number of patients with histological chronic hepatitis have transiently normal aminotransferase levels (David and Daniel, 2003). Also the results of the present study are similar to the study was done in Turkey and the researchers founds that serum mean ALT values were three to six times higher and the mean AST values were approximately three times higher in chronic hepatitis B (Kursad, et al., 2005). (Bonacini, et al., 1997) who are reported that the ALT is consistently higher than AST with chronic hepatic injury and these results are the same as in present study results. A minority of individuals with only one elevated ALT were found to have liver disease, while in patients with chronic HBV infection without elevated ALT “chronic carriers”, approximately 10% developed increased ALT (Kundrotas and Clement, 1993). (Veldhuijzen, et al., 2008) revealed that a single ALT determination can successfully predict viral load in chronic HBV patients and can be used in primary care to select patients for referral to specialist care. Sometimes patients with high serum HBV DNA can have a normal serum ALT activity. This occurs in cases known as immunotolerant HBV (Wang, et al., 2008). Aminotransferases are normally intracellular enzymes (mainly hepatic cells), and low levels found in the plasma represent the release of cellular contents during normal cells turnover, so elevation of plasma aminotransferases level indicates damage to cells rich in these enzymes, such as viral hepatitis (Pamela, et al., 2005).

4.10. AP:

The present study revealed that no significant differences in AP between patients and control group, and the mean values of AP for patients was (51.34±12.03 U/L), and for control group (50.43±9.99 U/L). In other words the elevation of AP in chronic HBV is unusual. This finding is in agreement with (Whitehead, et al., 1999); that showed elevation of AP above reference limit in less than 10% of examined cases and about

90% of those patients are of normal values. Another study done for uncomplicated hepatitis revealed that the elevation of AP above normal limit is present in less than 8% of examined cases (Doumas, et al., 2004). The mild elevation of serum AP in chronic HBV infection showed no significant statistical difference (Mark, et al., 1998) and (Vinay, et al., 2005).

4.11. TSB:

This study revealed that there were no significant statistical differences in mean values of TSB for patients (11.71±3.89 µmol /L), and control group (10.43±3.99 µmol /L), and this finding is consistent with (David and Daniel, 2003), who mentioned that, the serum bilirubin level is normal in chronic viral hepatitis. This finding indicate that the TSB didn't increase in chronic HBV infection which is different from an acute hepatitis B infection (when the jaundice develops in 33-50% of cases) as illustrated by (Gitlin, 1997). The bilirubin is metabolized in the liver and secreted via biliary ducts, so any defect in hepatocytes lead to increase in TSB, but in chronic HBV infection it is mildly elevated, as mentioned by (Vinay, et al., 2005), that is why no statistical difference between patients and controls was noticed.

4.12. FBS:

This study revealed that there is a significant difference between the mean values of FBS for patients (8.25±1.95 mmol/L), and control group, (4.24±0.61 mmol/L), which is in agreement with that mentioned by (Kassas, 1998) in which diabetes mellitus was significantly more frequent in chronic HBV cases. The present study was similar in it is finding to another study done by (Kwon, 2003) who found that the impaired glucose tolerance and overt DM frequently occurs in patients with chronic liver disease, and among the cirrhotic patients 57.1% had HBV related disease, and a DM was observed in 22.4% of the cirrhotic patients; and only 20.6% of the diabetic patients had normal range of blood glucose levels even though most of them received medical therapy. Also diabetic patients with well controlled blood glucose showed higher survival rate than poorly controlled cases. (Paraschiv, et al., 2002) found that the frequency of diabetes

and impaired glucose tolerance in chronic liver diseases was 30% in patients with HBV infection who showed an altered responds to a standard oral glucose tolerance test which was investigated in order to evaluate their pancreatic-endocrine features. The results of this study are in agreement with those obtained by (Ling, et al., 2007) who found that the prevalence of diabetes mellitus was significantly higher in patients with HBV than in those without HBV (58.9% vs. 33.3%), and the prevalence of diabetes mellitus in patients with HBV was significantly higher than in those without HBV among Asians (65.0% vs. 27.5%) but not in Pacific Islanders (43.8% vs. 37.1%), and in patients who were tested for HBV, the prevalence of diabetes mellitus was 44.4% in patients with HBV, and 85.0% in patients with HBV and HCV coinfection, so HBV infection is strongly associated with diabetes mellitus. The present study is also in agreement with the following studies: (Papatheodoridis, et al., 2006) found that the diabetes was present in (13%) of chronic hepatitis patients, without any difference between those with chronic hepatitis B (14%) or chronic hepatitis C (13%), and the presence of diabetes was independently associated with more severe fibrosis or presence of cirrhosis. (Imazeki, et al., 2008) found that the prevalence of DM in the chronic HBV, and chronic HCV groups was 6.3%, and 13.6%, respectively. (Kwon, et al., 2005) showed that the prevalence of DM was 19.7% in the HBV, and the DM would be detected before the diagnosis of cirrhosis or simultaneously in 79% of HBV. (Demir, et al., 2008) found that the HBV was detected in 11% of the diabetic patients and in 3% of the controls, these data suggest that the prevalence of occult HBV infection is higher in diabetics compared with healthy controls and this may contribute to the increased prevalence of primary hepatocellular carcinoma in diabetic patients. The explanation of these results as mentioned by (Kwon, 2003) is that hyperinsulinaemia and peripheral insulin resistance contribute to the development of DM in these patients. Patients with HBV infection showed signs of enhanced insulin resistance but overt diabetes develops in those who, in addition to insulin insensitivity, have a relative defect of insulin secretion which is the main mechanism leading to both glucose intolerance and overt diabetes (Paraschiv, et al., 2002).

Conclusions and Recommendations:

A. Conclusions:

1. Chronic HBV infection induces abnormal serum aminotransferases (ALT and AST) and no significant effect on AP and TSB.
2. The prevalence of chronic HBV infection increases among diabetic patients and chronic HBV infection may induce diabetes mellitus.
3.

B. Recommendations:

1. Chronic HBV should be considered to any patient presented with high serum transaminase (ALT and AST) while normal TSB and AP, not be excluded chronic HBV infection.
2. Blood glucose should be checked in any patient presented with chronic HBV infection and HBsAg should be done to any diabetic patient.
3. Because of high incidence of vertical transmission of chronic HBV infection, HBV vaccine should be given to any pregnant women mainly in the third trimester.

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